

Docket No.: 1422-0712PUS1  
(PATENT)

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In re Patent Application of:  
Kouichi KITAHATA et al.

Application No.: 10/571,582

Confirmation No.: 9795

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Art Unit: 1611

For: POROUS SILICA HAVING SUBSTANCE  
CARRIED THEREON

Examiner: NATHAN,  
Shyam

**DECLARATION UNDER 37 CFR 1.132**

COMMISSIONER FOR PATENTS  
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Sir:

I, Kouichi KITAHATA, residing in Mie-ken, Japan, hereby declares and states as follows:

1. That I am a co-inventor of the above-identified application, and thoroughly familiar with the contents of U.S. Application Serial No. 10/571,582 filed on March 10, 2006, entitled POROUS SILICA HAVING SUBSTANCE CARRIED THEREON, its prosecution before the United States Patent and Trademark Office and the references cited therein.

2. I am a graduate of The Kagoshima University, Faculty of Agriculture and received a master's degree in the year 1995, majoring in Biochemical Science and Technology.

3. That I have been employed in Taiyo Kagaku Co., Ltd. in the year 1996 and have been assigned to the Research Laboratories.

4. I have been involved in the research and development of mesoporous silica since 2003.

5. The following experiments were conducted by myself or under my direct supervision and control in order to compare and study the physical property and the sustained-release of porous silica of the present invention with those of Garlick (U.S. Patent No. 5,695,746).

#### EXPERIMENTAL METHOD

##### 1. Preparation of Porous Silica According to the Present Invention

Porous silica of the present invention was prepared according to the method of Preparation Example 1 of the present invention.

Specifically, 50 g of No. 1 sodium silicate ( $\text{SiO}_2/\text{Na}_2\text{O} = 2.00$ ) manufactured by Nippon Chemical Industrial Co., LTD, was dispersed in 1000 ml of a 0.1 M aqueous solution of octadecyltrimethylammonium chloride [ $\text{C}_{18}\text{H}_{37}\text{N}(\text{CH}_3)_3\text{Cl}$ ], a surfactant, and the dispersion was heated at 70°C for 3 hours while stirring. Thereafter, while heating the mixture at 70°C and stirring, a 2 N hydrochloric acid was added to the dispersion to lower its pH to 8.5, and the mixture was further heated at 70°C for 3 hours while stirring. A solid product was temporarily filtered and re-dispersed in 1000 ml of ion-exchanged water while stirring. The procedures of filtration and dispersion-stirring were repeated 5 times, and thereafter the residue was dried at 40°C for 24 hours. The

dried solid product was heated in nitrogen gas at 450°C for 3 hours, and thereafter the heated solid product was baked in air at 550°C for 6 hours to give a porous silica.

## 2. Porous Silica of Garlick

Porous Silica Syloid 63 and Syloid 244 (manufactured by W. R. Grace) were used.

## 3. Preparation of Menthol-Supporting Porous Silica

Each of the porous silica prepared above, Syloid 63 and Syloid 244 was dried over at 120°C for 2 hours. A solution prepared by dissolving 0.75 g of natural L-menthol in 10 ml of ethanol was added dropwise to 5 g of the dried porous silica while mixing, and allowed to stand for an hour. Thereafter, the solvent (ethanol) was removed by concentration with a rotary evaporator at 35°C for 30 minutes to give a power, and then the powder was dried over with a VACUUM DRYING OVEN (manufactured by ADVANTEC) under reduced pressure at 30°C for 120 minutes. Subsequently, the residue was further dried over at normal pressure at 36°C for 100 minutes to give a menthol-supporting porous silica.

## 4. Form of Pores and Specific Surface Area of Porous Silica

The form of pores was determined with a fully automatic X-ray diffractometer (RINT ULTIMA II, manufactured by Rigaku Denki K.K.). The specific surface area was obtained from the nitrogen adsorption isotherm determined according to a known BET method.

#### 5. Amount of Menthol Supported in Porous Silica

The amount of menthol supported in porous silica was determined as follows. The obtained a menthol-supporting porous silica was heated at 36°C to a temperature of 580°C for 120 minutes. Reduced weight of the menthol-supporting porous silica with heating was determined with Thermotic Analyzer. The determined reduced weight was assumed to be the amount of menthol supported in porous silica based on the silica on a solid basis.

#### 6. Sustained-Release of Porous Silica

The sustained-release of porous silica was evaluated as follows. The obtained a menthol-supporting porous silica was heated at 36°C to a temperature of 40°C at a rate of 0.01°C per minute. Reduced weight of the menthol-supporting porous silica with heating was determined with Thermotic Analyzer to give a release rate of a menthol per a menthol-supporting porous silica. The obtained release rate of a menthol was considered as the sustained-release of porous silica.

### RESULTS

#### 1. XRD Pattern of Porous Silica

According to the above method, XRD patterns of the prepared porous silica, Syloid 63 and Syloid 244 were obtained. The obtained XRD patterns were shown below.

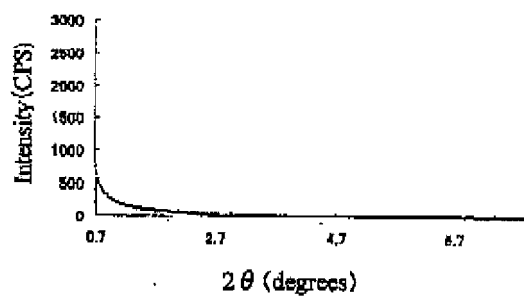


Fig. 1 (Syloid 63)

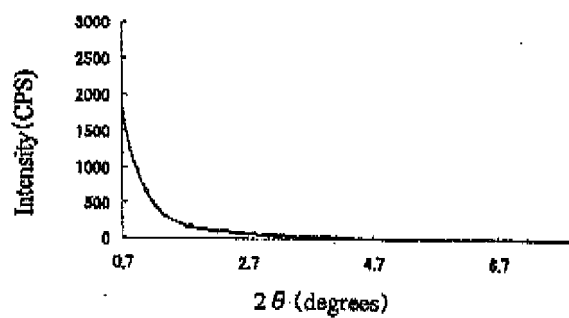


Fig. 2 (Syloid 244)

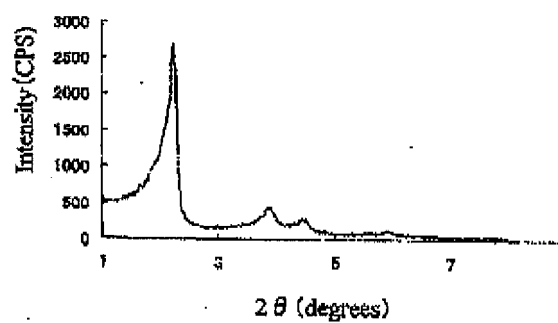


Fig. 3 (the porous silica of the present invention)

From Fig. 1 and Fig. 2, it was confirmed that pores having a non-hexagonal structure were formed in the porous silica of Syloid 63 and Syloid 244. On the other hand, it was confirmed that pores having a hexagonal structure were formed in the porous silica prepared according to the method of Preparation Example 1 of the present invention from Fig.3.

2. Comparison of Physical Properties and Sustained-Release of Porous Silica of the Present Invention with Those of Garlick

Physical properties and sustained-release of porous silica of the present invention, Syloid 63 and Syloid 244 were evaluated according to the above method. The results were summarized in Table 1.

Table 1

	Form of Pores	Specific Surface Area(m <sup>2</sup> /g)	Amount of Supported Menthol *	Release Rate of Menthol (mg/min)
Syloid 63	non-hexagonal	704	22.50	$48.6 \times 10^{-6}$
Syloid 244	non-hexagonal	297	15.50	$26.7 \times 10^{-6}$
porous silica	hexagonal	1020	17.90	$9.7 \times 10^{-6}$

\*: the values were expressed in % by weight based on the weight of porous silica on a solid basis.

From Table 1, it was confirmed that the porous silica according to the method of the present invention had a larger specific surface area than those of Syloid 63 and Syloid 244.

#### DISCUSSION

From Figs. 1 to 3 and Table 1, it is found that the porous silica of the present invention differs in structural feature from those of Garlick.

As to specific surface area, the porous silica according to the method of the present invention has a specific surface area falling within the range of 400 to 1500  $\text{m}^2/\text{g}$  of the present invention.

As to sustained-release, the release rate of menthol of the porous silica of the present invention is markedly slower than that of Garlick.

Therefore, it is found that the porous silica of the present invention can exhibit unexpectedly excellent sustained-release as compared with that of Garlick.

As is clear from the comparisons of structural feature and exhibited effect between porous silica of the present invention and that of Garlick, it is found that the porous silica of the present invention does not encompass the porous silica of Garlick.

**Statement Under 18 U.S.C. § 1001**

The undersigned petitioner declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Kouichi Kitahata

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Feb. 26, 2009

Date